

AMENDMENTS TO THE CLAIMS

Cancel claims 1-88 and add new claims. A complete listing of the claims in this case, with their status, is shown below.

1.-88. (Cancelled)

89. (New) A binding moiety comprising an extracellular cytokine binding domain consisting of a first FnIII-like domain and a second FnIII-like domain, wherein the cytokine binding domain comprises a modification which alters at least one property of the cytokine binding domain.

90. (New) The binding moiety according to claim 89, wherein the first and second FnIII-like domains are derived from the extracellular cytokine binding domains from separate sources.

91. (New) The binding moiety according to claim 89, wherein the first and/or second FnIII-like domain(s) is/are derived from the extracellular domain of a receptor selected from the group consisting of IL-2 receptor, IL-3 receptor, IL-4 receptor, IL-5 receptor, IL-6 receptor, IL-7 receptor, IL-9 receptor, IL-11 receptor, IL-12 receptor, IL-13 receptor, IL-15 receptor and IL-21 receptor, G-CSF receptor, GM-CSF receptor, LIF receptor, oncostatin M receptor, cardiotrophin CT-1 receptor, ciliary neurotrophic factor (CNTF) receptor, prolactin receptor, leptin receptor, erythropoietin receptor, growth hormone receptor, cytokine receptor-like factor 1, class 1 cytokine receptor, thymic stromal lymphopoietin protein receptor or gp130.

92. (New) The binding moiety according to claim 89, wherein at least one loop of the cytokine binding domain is modified such that, as compared with the corresponding loop in the unmodified cytokine binding domain;

- (i) the size or area, or both, of the loop is modified; or
- (ii) the size of the loop is increased or reduced by at least two amino acid residues; or
- (iii) the size of the loop is increased by at least 10 amino acid residues; or
- (iv) the size of the loop is increased by up to 20 amino acid residues.

93. (New) The binding moiety according to claim 92, wherein the at least one loop is in the binding interface of the FnIII-like domain.

94. (New) The binding moiety according to claim 89, wherein one or more of intra-domain disulphide-bond forming cysteine residues in the cytokine binding domain is/are modified

95. (New) The binding moiety according to claim 89, wherein the solubility of modified binding moiety is improved.

96. (New) The binding moiety according to claim 95, wherein the solubility of the binding moiety is improved by removing or replacing, or both, disulphide-bond forming cysteine residues within the cytokine binding domain.

97. (New) The binding moiety according to claim 89, wherein the affinity of the modified cytokine binding domain for at least one natural ligand of the unmodified cytokine binding domain is reduced or abolished or the binding specificity of the modified cytokine binding domain is different to that of the unmodified cytokine binding domain, or both.

98. (New) The binding moiety according to claim 97, wherein the unmodified cytokine binding domain is derived from the extracellular domain of a first receptor having specificity for a first ligand, one or more loops of the unmodified cytokine binding domain have been replaced with the corresponding loops of a second receptor having specificity for a second ligand, and the modified cytokine binding domain has specificity for the second ligand.

99. (New) The binding moiety according to claim 98, wherein the first receptor is IL-6 receptor and the second receptor is selected from the group consisting of prolactin receptor, LIF receptor and oncostatin M receptor.

100. (New) The binding moiety according to claim 89 linked to one or more diagnostic reagent(s) or therapeutic agent(s).

101. (New) A pharmaceutical composition comprising a binding moiety according to claim 89 and a pharmaceutically acceptable carrier or diluent.

102. (New) A polynucleotide library comprising a plurality of polynucleotides encoding binding moieties comprising a cytokine binding domain, which polynucleotides comprise one or more modifications in the cytokine binding domain.

103. (New) A method of selecting a binding moiety with an affinity for a target molecule which comprises

- (i) providing a plurality of polynucleotides according to claim 102;
- (ii) expressing the binding moieties encoded by the polynucleotides; and
- (iii) selecting one or more binding moieties having an affinity for the target molecule.

104. (New) The method according to claim 103, wherein the modification(s) is/are in the loop(s) of the cytokine binding domain.

105. (New) The method according to claim 103, wherein the plurality of nucleotides are generated by synthesising a plurality of random synthetic oligonucleotides and inserting the oligonucleotides into a sequence encoding the binding moiety.

106. (New) A method according to claim 103, wherein the target molecule is a cytokine receptor ligand.